ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

Location of Meeting
Frontier Building, 3601 C Street, Room 890/896

FINAL MINUTES OF MEETING
November 19, 2010
8:00 a.m.

Committee Members Present:
Amber L. Briggs, Pharm.D.
Richard E. Brodsky, MD
Robert H. Carlson, MD
Jeffrey G. Demain, MD
Vincent Greear, R.Ph. (telephonic)
Diane Liljegren, MD (telephonic)
Paul Michaud, Pharm.D.
John E. Pappenheim, MD
Claudia Phillips, MD
Jill Reid, R.Ph. (telephonic)
Janice Stables, MSN, ANP (telephonic)

Committee Members Absent:
Dharma Begich, Pharm.D.
Marvin Bergeson, MD
Daniel P. Kiley, DDS MPH
Andrew Maciejewski, MD
Sherrie D. Richey, MD
Trish White, R.Ph.

Others Present:
David Campana, R.Ph.
Alex Malter, MD MPH
Chad Hope, Pharm.D.
Julie A. Pritchard, Pharm.D.

1. Call to Order – Chair

Chair Brodsky called the meeting to order at 8:03 a.m.

2. Roll Call

A quorum was present. Dr. Julie Pritchard has replaced Dr. Melinda Sater.

3. Public Comments

DR. DAVID SAMPSON: A psychiatrist, discussed the atypical antipsychotic medications. Since the last review, Saphris, Fanapt, Zyprexa, and Relprevv, the long-term injectable formulations, have been added. All the atypical medications are used when treating bipolar disorder as schizophrenia. All of the medications are very distinct. Alaska Medicaid recipients should have access to all new and existing

antipsychotics, both typical and atypical. There is a "fear factor" associated with Relprevv, which is identical to Zyprexa oral in its effects and side effects, except it is a two- to four-week long-term injectable. It differs from existing long-term injectables in that it is a Zyprexa product, which means it avoids some of the EPS-type problems. Some clinicians and pharmacists are fearful of the post-injection delirium or sedation syndrome that happens in less than 1 percent of the patients who receive this medication. Patients are required to remain in a clinical setting for observation three hours after injection to ensure the sedation problem does not occur. It is not a toxicity problem. In rare cases as far as coma, it totally resolves within a matter of three days and usually much less. All of the atypical antipsychotics, as well as the new long-term injectable Relprevv, should be included on the PDL for the benefit of schizophrenic and bipolar patients.

4. Review of Tramadol Agents (Red Category)

Dr. Pritchard gave the Magellen presentation on Tramadol Agents. Tramadol is a centrally acting analgesic with both opioid and non-opioid properties. It also weakly inhibits norepinephrine and serotonin reuptake. This class now includes Ryzolt, Ultram ER, Tramadol, Ultram, Rybix ODT, and Ultracet. Ryzolt ER and Ultram ER are non-scheduled options for once-daily pain control. Although these are not scheduled drugs, they are contraindicated where opioids are contraindicated. In addition, discontinuation needs to be via tapering to avoid withdrawal symptoms. Tramadol products should not be used with SSRIs. They are not for use in children under age 16.They are metabolized through the CYP450 pathway and should not be used in patients that are on Carbamazepine, because the result is greatly reduced pain relief. In October, there were 615 claims: 92.5% for Tramadol, 3.9% for Tramadol with acetaminophen, 1.79% for Ryzolt, 1.3% for Ultram ER, and 0.49% for Ultram. This is a new class and has not been reviewed. The Ryzolt study showed greater reduction in pain in patients with osteoarthritis, but more patients dropped out of the study due to adverse effects with Ryzolt than placebo. Rybix ODT is for management of moderate to severe pain in adults, but no studies show any quicker onset of action with ODT versus regular release. There was no expert opinion on this class.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTICALLY EQUIVALENT, AND AT LEAST ONE SHORT-ACTING PREPARATION BE INCLUDED ON THE PDL. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.

5. Re-Review of Statins (Red Category)

ERIKA SZABO: A representative of Eli Lilly discussed Livalo. First, I am required to state the following. See full prescribing information. Pitavastatin is contraindicated in patients with active liver disease, women who are pregnant or may become pregnant, nursing mothers, co-administration with cyclosporine, and those with known hypersensitivity to product components. Patients should be advised to promptly report unexpected muscle pain, tenderness, and weakness, and discontinue Pitavastatin if signs or symptoms of skeletal muscle (indiscernible) appear. Risk increases in a dose-dependent manner with advanced stage renal impairment and inadequate treatment of hyperthyroid. Persistent elevation in hepatic transaminase can occur. Monitor liver enzymes before and during treatment. Since 2003, Livalo has been approved in Japan and other countries. It is a statin for those with primary hyperlipidemia and mixed dyslipidemia as an adjunctive therapy to diet to reduce total cholesterol, LDLs, triglycerides and HDLs. Its starting dose is 2 milligrams with a maximum dose of 4 milligrams. The reason for bringing another statin to the market was discussed. Livalo is simply another option for these patients to reach goal. The unique metabolism of Livalo was discussed.

Several studies and their outcomes were reviewed. In summary, Livalo achieved comparable LDL-C reductions compared to Atorvastatin and Simvastatin. It had significantly greater LDL-C lowering versus Pravastatin. Efficacy and safety was established in a variety of patient populations, including those with primary hyperlipidemia, mixed dyslipidemia, diabetes, multiple cardiovascular risk factors, and the elderly. Livalo had no significant effect on PT and INR when administered in patients receiving chronic Warfarin treatment.

In response to Dr. Hope's question on renal dosing requirements, Ms. Szabo said the package insert be consulted for that information.

DR. VICK VENSON: A representative of Merck discussed Ezetimibe (Vytorin). A compelling body of evidence shows that the lower the LDL level is, the lower the CVD event rate. This has been shown in epidemiologic observational studies, as well as a variety of interventional studies with a variety of agents done in many thousands of subjects. This is not only an epidemiologic observation, but has been confirmed in interventional randomized controlled trials. This has been shown to occur with many different methods of LDL lowering. Vytorin has been shown in separate head-to-head clinical studies to lower LDL more than Simvastatin, Atorvastatin, and Rosuvastatin at comparable doses. Two of those studies and their outcomes were reviewed. Atorvastatin and Rosuvastatin are the two strongest statins available, yet Vytorin, in head-to-head studies, lowered LDL more than each of them did. Ezetimibe, which blocks cholesterol absorption, has been shown by itself to reduce LDL about 18 percent, which is equivalent to three doublings of any dose of any statin. In summary, there is robust evidence that the Ezetimibe/Simvastatin combination, Vytorin, lowers LDL at least as much, and probably more, than any available statin. If you believe that lowered LDL lowers ischemic cardiovascular events, which is generally accepted throughout the world, then it makes since to include Vytorin on the PDL.

In response to Dr. Brodsky's question about whether Ezetimibe had translated into reduction in events or mortality, Dr. Venson discussed the ongoing IMPROVE trial, which is due to be completed in 2013. In that trial, 22 percent of the population had a reduction in events with Vytorin. Another trial showed that people with mild to moderate aortic stenosis had ischemic event reductions of 36 and 47 percent respectively.

DR. JAMES HURST: A representative of AstraZeneca discussed Crestor. In October 2009 and based on the PLUTO trial, the FDA approved the use of Crestor in pediatric patients ages 10 to 17 with heterozygous familial hypercholesterolemia. In February 2010, the FDA approved the use of Crestor to lower heart attack, stroke, and arterial revascularizations in individuals without clinically evident coronary heart disease, but an increase of cardiovascular disease based on age, greater than or equal to 50 in men and greater than or equal to 60 in women; HSCRP greater or equal to 2; and the presence of at least one additional cardiovascular risk factor including hypertension, lower HDL, smoking, or family history of premature coronary heart disease. This indication is based on the JUPITER trial, which studied 17,802 patients. The JUPITER trial and its outcomes were reviewed. Crestor has demonstrated to be highly efficacious at lowering LDL, raising HDL, and slowing the progression of arthrosclerosis.

Dr. Pritchard gave the Magellen presentation on Statins. The high potency statins are Atorvastatin, Rosuvastatin, Simvastatin and Vytorin. All of the agents are indicated for the treatment of hyperlipidemia. Other indications vary by product. In October, there were 1,906 claims: 47.58 percent

each for Lovastatin and Pravastatin, 2.23% for Lescol, 1.49% for Altoprev, .74% for Pravachol, and 0.27% for Advicor. Under the potency statins, there was 50.67% for Simvastatin, 20.77% for Lipitor, 19.73% for Crestor, 8.7% for Vytorin, and 0.12% for Zocor. Caduet, as the combination product, had five prescriptions. At the last review, a motion for class effect, to include at least one high-potency agent, passed unanimously. Since the last review, Livalo has been placed on the market. It is contraindicated with Cyclosporine. In doses greater than 4 milligrams a day, it shows a high risk of severe myopathy. Plasma concentrations of Livalo were found to be lower in healthy African Americans versus their healthy Caucasian counterparts. Livalo is usually compared to Pravastatin, Simvastatin and Atorvastatin. Other significant changes included the FDA issued a warning of increased muscle injury with the highest dose of Simvastatin, noted that the combination of Crestor and Gemfibrozil should be avoided, and to be aware of Crestor used in conjunction with some of the HIV drugs or Cyclosporine. There is no expert opinion on this class.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTICALLY EQUIVALENT, AND AT LEAST ONE HIGH-POTENCY STATIN BE INCLUDED ON THE PDL. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.

6. Review of Long-Acting Injectable Antipsychotics (Red Category)

ERIKA SZABO: A representative of Eli Lilly discussed Relprevv. I am required to state the following. See full prescribing information. Relprevv has a boxed warning for post injection delirium sedation syndrome and increased mortality in elderly patients with dementia related psychosis. Relprevv is not indicated for the use in this patient population. Patients are at severe risk from sedation, including coma and delirium, after injection and therefore must be observed for three hours with ready access to emergency response services. Close supervision for patients at high risk of suicide should accompany drug therapy. They should be monitored for signs of hyperglycemia, hyperlipidemia, and weight gain at the beginning of and periodically through treatment. In some cases, ketoacidosis and hyperosmolar coma or death have been associated with treatment. Narcoleptic malignant syndrome and tardive dyskinesia have been reported. Patient experiencing signs or symptoms of either should be managed with immediate discontinuation and close monitoring. Orthostatic hypotension may occur, especially during initial dose titration. Use with caution in those with cardiovascular, cerebrovascular disease, and conditions that could affect hemodynamic responses. Leukopenia, neutropenia, and agranulocytosis have been reported. Those with a history should have CBCs monitored frequently during the first few months. Discontinuation should be considered at the first sign of a clinically significant decline in white blood cells. Use cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold. Prolactin levels may be elevated. Relprevv's efficacy was established in two clinical trials in patients with schizophrenia. Two recent studies and their outcomes were reviewed. The risk benefit profiles suggest that Relprevv may be an important treatment option for patients with schizophrenia who struggle with non-adherence to oral antipsychotic medication.

In response to Dr. Demain, Ms. Szabo said patients who might have difficulty with using oral medications on a regular basis would benefit from using the injectable, which is administered every two to four weeks depending on the dose.

Dr. Pritchard gave the Magellen presentation on Long-Acting Injectable Antipsychotics. This class includes the first- and second-generation injectables. The first generations work primarily by blockade

of the dopamine-2 receptors in the mesolimbic dopamine pathway. The second generations work more in the serotonin dopamine area, which leads to a reduced incidence of EPS and increased efficacy for negative symptoms. They have been found to cause little to no elevation of prolactin levels. They seem to improve positive symptoms in schizophrenia, and to improve mood and decrease suicide in both bipolar and schizophrenic patients. There are still serious adverse effects with these drugs, which can include EPS, sedation, weight gain, metabolic issues, and anticholinergic effects, along with hypotension. Safety and efficacy of injectables in the pediatric population has not been established. In October, there were 58 claims: 60.3% for Risperdal Consta, 25.9% for Haldol, 12.1% for Fluphenazine, and 1.72% for Invega Sustenna. This is a new class so there was no previous discussion. Significant changes were reviewed. Invega Sustenna and Zyprexa Relprevv are approved for the maintenance treatment of schizophrenia. Relprevv has a boxed warning for risk of severe sedation, including coma and/or delirium. Patients need to be monitored in a health care facility for at least three hours after injection. There is inconclusive evidence that the overall effectiveness of the second-generation drugs is better than the first generation drugs. The EPS risk is decreased, but long-term adverse effects from the second generation are unknown. No studies say which product to use first. Generally, the adverse event profile can be used as a guide to therapy. Dr. Love from Alaska Psychiatric Institute says that they have extensive experience utilizing injectable long-acting formulations of Haloperidol, Risperidone, and Fluphenazine. The medical staff there held a series of discussions regarding personal experience, outpatient use, and literature reviews and determined that they will not add Invega Sustenna or Zyprexa to the in-house formulary. It is felt that those medications are more tailored to the outpatient setting. They do want keep Haldol, Fluphenazine, and Risperdal Consta available.

In response to Dr. Brodsky, Mr. Campana said the committee was only considering the long-acting injectable antipsychotics.

In response to Dr. Briggs' question regarding long-acting drugs that require REMs monitoring, Mr. Campana said no information has been received on the REMs, but the pharmaceutical people could probably fill us in on how that works for patients.

Dr. Liljegren discussed how disabling schizophrenia was and it affected patient, their family, and society. The response to a given medication is unpredictable enough that all of the long-acting drugs should be available.

Dr. Pappenheim discussed the equivalency between Fluphenazine, Haldol, and Risperdal, which are equivalent from a clinical standpoint. Long-acting Olanzapine is the only one that truly acts like an atypical antipsychotic and it would make sense to include it on the PDL.

Dr. Carlson pointed out that this was a very small group of difficult to manage patients. Most of the therapy is probably going to be initiated at API, and the PDL should make it easy for them to function. Dr. Brodsky responded that the medically necessary clause could always be utilized.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTICALLY EQUIVALENT. LONG-ACTING OLANZAPINE SHOULD BE INCLUDED ON THE PDL. SECONDED BY MS. STABLES.

Dr. Liljegren felt the motion should include at least one first generation injectable.

Dr. Demain discussed side effects and allergic reactions, which are difficult to manage when an injectable is used, because the drugs are in the patients' system for two to four weeks. Dr. Pappenheim explained that prescribers typically prescribed long-acting injectables only after a patient had been stabilized on the oral preparation and had a history of non-compliance.

Dr. Michaud questioned why Zyprexa Relprevv (Olanzapine) was included in the motion since there have been no prescriptions for the drug.

The committee discussed the medically necessary clause in relation to drugs that were used in facilities. Mr. Campana said the same rules applied as the normal outpatient prescriptions.

Dr. Pappenheim explained why the motion included (Olanzapine). From a clinical standpoint, it is significantly different in terms of the side effect profile and people being able to tolerate it. There is a subset of patients who will not do well on the other drugs, but they do well with Zyprexa, but have problems with adherence. The reason there were no prescriptions for the drug is probably that it is so newly available. Dr. Michaud responded that the medically necessary clause could be used for it and it did not need to be included in the motion.

Dr. Briggs felt it was reasonable to include one first generation and one-second generation drug on the PDL and not name a specific drug.

DR. PAPPENHEIM WITHDREW HIS MOTION.

DR. BRIGGS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTICALLY EQUIVALENT. ONE FIRST GENERATION AND ONE SECOND GENERATION LONG-ACTING ANTIPSYCHOTIC BE INCLUDED ON THE PDL. SECONDED BY DR. MICHAUD. THE MOTION PASSED UNANIMOUSLY.

7. Review of Suboxone

DR. TONY TOMASELLO: A representative of Reckitt Benckifer Pharmaceutical discussed Suboxone. The molecule Buprenorphine is a derivative opioid with high affinity at the mu-opioid receptor with low intrinsic activity and slow dissociation. It is also a kappa-opioid antagonist. Metabolism is by the CYP3A4 system, but no significant interactions have been reported. The bioavailability of Buprenorphine is 60 percent by the sublingual route, but only 10 percent when swallowed, so it is a sublingually administered product. It has a significant safety profile in that respiratory depression does not reach fatal levels. The treatment of opioid dependence with the product Suboxone or Subutex is authorized by the Drug Addiction Treatment Act passed by the U.S. Congress in 2000. Physicians authorized under this act can prescribe Buprenorphine or Buprenorphine/Naloxone combination products for opioid addiction treatment. This is the only medication authorized under the Drug Addiction Treatment Act of 2000 for this purpose. It is a schedule three controlled, dangerous substance under the Comprehensive Drug Abuse Control Act. Addiction is considered a chronic, primary, relapsing, fatal disease with biological roots and destructive behavioral consequences. Medication assisted therapy has been shown to retain people in treatment and to produce significant improvements in health and reductions in criminal behavior and the abuse of illicit drugs. The partial opioid agonist effect of Buprenorphine has to be used with caution by the physicians who prescribe it.

There are three Buprenorphine products, which were reviewed. Buprenorphine in combination with Benzodiazepines has been shown to lead to fatal respiratory depression. Patients must be warned that the abuse of Benzodiazepines, in combination with Buprenorphine, can be fatal. There is also a caution that Buprenorphine, although it is only a partial mu-agonist, does have abuse potential. The company is a very committed community partner in regards to mitigating abuse potential through their REMs program. We monitor patients, physicians, and treatment programs to determine whether Buprenorphine is a problem in the community. We identify physicians we believe are at risk physicians and we visit them to try to encourage them to follow the established guidelines.

In response to Dr. Liljegren's a question of whether Buprenorphine was indicated for pain control, Dr. Tomasello said that was a different product, possibly a transdermal patch, and he was not prepared to talk about another company's product. Suboxone and Subutex are only indicated for the treatment of opioid dependence.

In response to Dr. Demain's question regarding patients with an acute injury or upcoming surgery, Dr. Tomasello said there were guidelines for dealing for planned surgeries and both acute and chronic pain in opioid dependent patients treated with Suboxone. The half-life of Suboxone is about 32 hours, so patients who discontinue the medication can take advantage of full agonists later on. The Naloxone component is insignificantly absorbed by the sublingual route. Buprenorphine is a partial agonist. At 16-milligram doses, it occupies about 92 percent of opioid receptors. If a patient has a planned surgery that will require analgesic effects, they can discontinue Suboxone prior to the planned surgery and reengage treatment after the process.

Dr. Pritchard gave the Magellen presentation on Suboxone. Buprenorphine is a schedule three used in the sublingual form as an effective treatment for opioid dependence. Subutex is Buprenorphine alone and Suboxone is the combination of Buprenorphine and Naloxone. Prescribers need to have special recognition to prescribe Buprenorphine, known in pharmacy as the X number. It exerts activity at both the mu-receptor as an agonist and the kappa as an antagonist. It is 96 percent protein bound and goes through the CYP3A4 enzyme system. It does go to an active metabolite, which is Norbuprenorphine. It has not been studied in children under age 16 and treatment is always in conjunction with psychosocial therapy and addiction treatment programs. In October, there were 242 claims: 97.5% for Suboxone and 2.48% for Subutex. This is a new class so there was no previous discussion. Suboxone and Subutex are sublingual. You hold it under the tongue for five to ten minutes. Subutex is recommended for induction due to no Naloxone component then switched to Suboxone for maintenance. Sublingual is the preferred route as swallowing reduced bioavailability. Dr. Charles Herndon, the medical director of Providence Breakthrough, says he has been using Suboxone primarily, and some Subutex, since 2004. These drugs are literal lifesavers for opioid dependent persons. The sublingual form is not FDA approved for pain relief. Suboxone and Subutex, along with behavioral treatment, save lives both physically and socially. Even though these drugs are expensive, they are much more cost effective than jail or hospital care.

In response to Dr. Demain, Dr. Pritchard said Suboxone was a combination product. It is recommended that you use the Buprenorphine product for induction and then transition to the combination product for maintenance.

In response to Dr. Malter's question about long-term studies on efficacy and outcome studies, Dr. Pritchard said Dr. Herndon has treated more than 200 patients and said a very high percentage of those

had remained opioid addiction free for six years or more. He also noted that these drugs were needed long-term, and lifetime for some patients.

Dr. Carlson discussed the need to be selective in which patients received these drugs. If you medicate everyone, your results will be inferior to using them on a highly motivated group.

Dr. Pappenheim said induction was typically done with Suboxone. Subutex is used if a patient has a known allergy to Naloxone or is pregnant. Suboxone is more commonly used, but you want to include the Naloxone component so the substance is less likely to be abused.

Dr. Hope said Subutex was generic, but it does not have the Naloxone that severely limits its use.

Dr. Pappenheim said there were no good studies to show the effectiveness of the long-term use of the drug, although it is effective in the short-term for detoxing an opioid dependent patient. There is clearly a significant problem with the drug nationwide.

Dr. Liljegren suggested that this might be a medication that should always be prescribed using the medically necessary clause. Dr. Brodsky said it might be advantageous to have it on the list so the price could be reduced through the bid process.

The committee discussed how to word the motion, including the possibility of breaking it into two different classes.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BRIGGS. THE MOTION PASSED WITH ONE OPPOSED.

8. Review of Selective Constipation Agents (Red Category)

DR. SDUSKIE (PH): A representative of Takeda discussed Amitiza (Lubiprostone). Amitiza is FDA approved for the treatment of chronic idiopathic constipation, including those individuals over the age of 65, as well as for the treatment for irritable bowel syndrome associated with constipation (IBSC) for women older than 18 years old. Chronic constipation is estimated to effect between 12 and 19 percent of the population with increased prevalence in women and those over 65 years of age. IBSC is a common disorder that is characterized by abdominal pain and altered bowel habits associated with constipation that persists for at least three months when no structural or biochemical abnormalities are present. Amitiza is unique in the fact that it has a novel mechanism of action, which was reviewed. It works by increasing intestinal fluid, which increases motility, thereby increasing the passage of stool and alleviating symptoms associated with chronic idiopathic constipation or IBSC. It is also important to point out that it has low systemic absorption with plasma concentrations below the level that can be readily quantified because it is mostly metabolized while in the stomach and small intestine. There are no known P450 drug interactions associated with Amitiza. It has a pregnancy category of C so caution should be used for pregnant women who are prescribed this medication. Several clinical trials and their outcomes were reviewed. In a 2009 publication, a systematic review of the management of irritable bowel syndrome was conducted and gave Lubiprostone, in the dose of 8 micrograms twice daily for the treatment of IBSC, a 1-B rating, which is the second highest rating for clinical evidence.

Dr. Pritchard gave the Magellen presentation on Selective Constipation Agents. As that is the only drug in the class, Dr. Sduskie just reviewed the information. Other drugs used for constipation are the OTC products, which are divided into the fiber laxatives, saline laxatives, osmotic laxatives, and stimulant laxatives. However, for this class, Amitiza is the only product up for review. In October, there were 24 claims. This is a new class so there was no previous discussion. Amitiza should be reserved for use in those who have failed other treatment options for constipation.

DR. LILJEGREN MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS.

In response to Dr. Demain's question of whether this drug would require prior approval, Mr. Campana said this class could have a step edit that would require trying OTC laxatives first. OTC laxatives are available through the Medicaid program without restriction.

THE MOTION PASSED WITH ONE OPPOSED.

9. Re-review of Long-Acting Opioids (Blue Category)

There were no testimonies.

Dr. Pritchard gave the Magellen presentation on Long-Acting Opioids. Many of these products carry black box warnings regarding extreme potency abuse potential in overdose. In October, there were 558 claims: 32.4% for OxyContin, 25.8% for Morphine Sulfate Sustained Action, 20.43% for Fentanyl, 8.42% for Kadian, 4.12% for Oxycodone 12-Hour, 2.87% for Avinza, 2.33% for Embeda, 1.97% for Opana ER, 0.9% for Duragesic, and 0.72% for MS Contin. At the last review, a motion for a class effect to include Methadone and one transdermal preparation, passed unanimously. Significant changes were reviewed. Exalgo, which is the hydromorphone extended release, was added to the market. It is for use in those requiring continuous analgesia for moderate to severe pain for extended time periods. It is contraindicated in patients with acute or severe respiratory conditions, paralytic ileus, or narrow or obstructed GI tract. Hydromorphone has a black box warning of not for use in those opioid naive patients and do not break, chew, or crush the tablets, as rapid release could be fatal. Embeda has a do not crush or chew warning. In the OxyContin update, the new formulation to reduce immediate access to the full dose is due out. When that is released, the manufacturer will cease shipping the original OxyContin formulation. The currently preferred drugs are Morphine Sulfate, Kadian, Opana, Duragesic and Oramorph SR.

In response to Dr. Malter, Mr. Campana said Methadone is on the PDL and would be included in this discussion.

DR. CARLSON MOVED A CLASS EFFECT TO INCLUDE METHADONE AND ONE TRANSDERMAL PREPARATION. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.

10. Re-Review of Fentanyl, Buccal (Blue Category)

There were no public testimonies.

Dr. Pritchard gave the Magellen presentation Fentanyl, Buccal. On the short-acting narcotic is Fentanyl. The Buccal formulations are Fentora and Onsolis. The transmucosal formulation of Actiq. Nucynta is new to the class and may act by inhibiting norepinephrine reuptake, along with activity at the mu-opioid receptors. All agents require prior authorization and are use only in opioid tolerant patients. In October, there were 13 claims: 76.92% for Nucynta, 66.67% for Fentora, and 33.33% for Fentanyl Citrate. At the last review, a motion for class effect passed with one opposed. The significant changes were reviewed. Nucynta was compared to both Morphine IR and Oxycodone. The incidents of nausea and vomiting seemed lower, but not statistically significant compared to Morphine. However, nausea, vomiting, and constipation were significantly lowered when compared to Oxycodone. Pain relief was similar in all the studies.

DR. LILJEGREN MOVED A CLASS EFFECT. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

11. Re-review of Anticonvulsants, 1st Generation (Blue Category)

There were no public testimonies.

Dr. Pritchard gave the Magellen presentation Anticonvulsants. These drugs are broken down by Carbamazepine derivatives, first generation, and second generation. There are many different dosage forms, both branded and generic products. Mechanisms are not clearly understood for some and mechanism of action can vary widely between agents. In October, there were 4,201 claims: 658 were for the Carbamazepine derivatives, 2,544 for the second generation, and 1,003 for first generation. At the last review, a motion for therapeutic alternatives for the first generation drugs passed with two opposed. A motion for therapeutic alternatives with no preference for the second-generation drugs passed with three opposed. The significant changes were reviewed. Sabril received an indication for infantile spasms, but it can cause irreversible vision loss. If clinical improvement is not seen in two to four weeks, the product should be discontinued. Vision screening is required at baseline and every three months. This drug is only available through a special restricted distribution program called the Share Program.

Mr. Campana noted that there was public testimony for anticonvulsants, second generation.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

12. Re-review OF Anticonvulsants, 2nd Generation (Blue Category)

NIGEL ISACK (PH): A representative of UCB discussed Vimpat. Despite the availability of more than 20 anti-epileptic drugs on the market, approximately one-third of patients with epilepsy still have uncontrolled seizures and/or intolerable side effects on their current therapy. This represents an unmet need for patients and their caregivers and more therapeutic options are necessary. Vimpat has the first novel mechanism of action, which was reviewed. Vimpat is a new second generation that is a sodium channel modulator, specifically affecting the slow inactivation of sodium channels. The efficacy and safety of Vimpat has been studied extensively in more than 1,300 patients in three randomized double-blind placebo controlled trials, which were reviewed. Vimpat is generally well tolerable, adverse events are generally mild to moderate and dose dependent. The most common adverse effects were

reviewed. In clinical trials, rates of discontinuation due to adverse effects were low. No laboratory monitoring is required. Vimpat is indicated as adjunctive therapy in the management of partial onset seizures in patients 17 years of age or older with epilepsy. It is available as oral tablets and an injection for intravenous use.

Dr. Pritchard gave the Magellen presentation Anticonvulsants, second generation. In October, there were 2,540 claims: 14 claims for Vimpat, the largest use were Gabapentin at 818. At the last review, a motion for therapeutic alternatives with no preference passed with three opposed.

DR. DEMAIN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES WITHOUT PREFERENCE. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

13. Re-review of SNRIs (Blue Category)

ERIKA SZABO: A representative of Eli Lilly discussed Cymbalta. I am required to state the following. See full prescribing information. Cymbalta has a boxed warning for increased risk of suicide thinking and behavior in children, adolescents and young adults taking antidepressants for MDD and other psychiatric disorders. Patients of all ages started on therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. It is not approved for pediatric patients. Those taking MOIs or who have uncontrolled narrow angle glaucoma should not take Cymbalta. At least 14 days should elapse between discontinuing an MOI and starting Cymbalta. At least five days should be allowed after stopping Cymbalta before starting an MOI. Hepatic failure, sometimes fatal, has been reported. Cymbalta should be discontinued in patients who develop jaundice or other evidence of clinically significant liver dysfunction and should not be resumed unless another cause can be established. It should not be prescribed for those who have substantial alcohol use or evidence of chronic liver disease. Taking Cymbalta with NSAIDS, aspirin, or blood thinners may increase bleed risk. Serotonin symptom or NMS-like reactions have been reported with SSRIs and SNRIs. If seen, discontinue Cymbalta and initiate supportive therapy. Cases of orthostatic hypotension have been reported. Monitor blood pressure prior to initiating treatment and periodically throughout treatment. Cymbalta has an established safety profile across multiple indications, which were reviewed. The recommendation for all of these indications is 60 milligrams per day. Today, my focus will be on MDD and chronic pain. MDD's treatment goals should be remission. It is important to treat patients to full remission, because patients who fail to achieve remission face a higher risk of relapse. Therefore, adherence and persistence is important. A 2009 analysis of Cymbalta, Effexor XR, Lexapro and three generic SSRIs concluded that Cymbalta patients were more adherent and persistent than those on the other drugs. Cymbalta can effectively treat chronic pain, regardless of its origin, since it is a centrally acting analgesic as supported by its approved indications. Several studies and their outcomes were reviewed. Cymbalta gained its muscular skeletal pain indication from data on chronic lower back pain and osteoarthritis. Studies show that Cymbalta back pain patients use less pain treatments, such as opioid, NSAIDs, skeletal muscle relaxing meds, and had lower rates of surgery in non-evasive treatments. Cymbalta offers an alternative to pain treatment, which is non-opioid, non-narcotic, and non-NSAID.

Dr. Pritchard gave the Magellen presentation on SNRIs. There are many different products, both ER and IR. The mechanisms of action differ between agents, as do the ADRs and indications in therapeutic uses. In October, there were 1,124 claims: 51.42% for Cymbalta, 23.49% for Venlafaxine

ER, 8.36% for Pristiq, 6.58% for Effexor XR, 3.56% for Savella, 3.38% for Venlafaxine 24, and 3.2% for Venlafaxine. At the last review, a motion for therapeutic alternatives, to include at least one of the fibromyalgia medications, passed unanimously. The significant changes were reviewed. SNRIs are second line for panic disorder. The FDA requires a medication guide to be supplied with Venlafaxine.

In response to Dr. Brodsky, Dr. Pritchard said the fibromyalgia medications were Savella and Cymbalta.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES AND AT LEAST ONE FIBROMYALGIA MEDICATION WOULD BE INCLUDED ON THE PDL. SECONDED BY DR. PAPPENHEIM.

In response to Dr. Carlson, Mr. Campana explained that class effect or therapeutic alternatives would have the same result. The committee further discussed the difference between class effect and therapeutic alternatives and how that would affect practitioners.

THE MOTION PASSED WITH ONE OPPOSED.

Break from 9:44 a.m. to 10:40 a.m.

Dr. Brodsky noted that when the Fentanyl, Buccal class was reviewed, Nucynta was listed, but was not considered in that class and will be considered at another time.

14. Re-review of Atypical Antipsychotics (Blue Category)

DAVE GROSS: A representative of Pfizer discussed Geodon. Geodon provides proven efficacy in the treating of both the positive and negative symptoms of schizophrenia, the acute exacerbation of symptoms in both schizophrenia and schizoaffective disorder, and the prevention of relapse with long-term use. Geodon is also indicated for patients with acute manic or mixed episode with or without psychotic features associated with bipolar disorder. Since the last review, it has a new indication for the maintenance treatment of bipolar disorder as an adjunct to Lithium or Valproic Acid. Geodon has a well-established safety and favorable tolerability profile with neutral effects, and in some cases improvement, relative to other atypical antipsychotics on weight and metabolic parameters. It has both oral and IM formulations. Geodon intra-muscular is not a long-acting atypical antipsychotic. It is short acting and is typically used in acute agitation for schizophrenia. A six-month study in patients with manic or mixed symptoms of bipolar I disorder with or without psychotic features was reviewed. Geodon is not associated with weight gain, hyperlipidemia, or elevated plasma glucose levels. In summary, Geodon has several therapeutic benefits and proven advantages over other agents in this class. It provides powerful efficacy without compromising overall patient health. It is well recognized by researchers and physicians that there exist many differences amongst atypical antipsychotics. We firmly believe it is very important to have open access to atypical antipsychotics so clinicians can provide the best care for their patients and match the appropriate medicine to an individual patient.

ERIKA SZABO: A representative of Eli Lilly discussed Zyprexa and Zydis. I am required to state the following. See full prescribing information. Zyprexa has a boxed warning for increased mortality in elderly patients with dementia related psychosis. It is not indicated for the use in this patient population. Close supervision for patients at high risk for suicide should accompany drug therapy.

Patients should also be monitored for signs of hyperglycemia, hyperlipidemia, and weight gain at the beginning and during treatment. In some cases, ketoacidosis and hyperosmolar coma or death have been associated with treatment. Neuroleptic malignant syndrome and tardive dyskinesia has been reported. Patients experiencing signs of symptoms of either should be managed with immediate discontinuation and close monitoring. Orthostatic hypotension may occur, especially during initial dose titration. Use with caution in patients with cardiovascular, cerebrovascular disease, and conditions that could affect hemodynamic responses. Leukopenia, neutropenia, and agranulocytosis have been reported. Those with a history should have CBCs monitored frequently during the first few months. Discontinuation should be considered at the first sign of a clinically significant decline in white blood cells. Use cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold. Prolactin levels may be elevated. Since Zyprexa's approval 14 years ago, Lilly continues to monitor its efficacy and safety. Next year, Zyprexa's patent will expire. Two meta-analysis studies on and their outcomes were reviewed. Schizophrenia afflicts patients for life and even a small benefit may be important. There are substantial differences between individual patients and how they respond to these drugs. The balancing of efficacy and side effects must be tailored to the individual patient, setting, and health care system. Zyprexa and Zydis should be considered for inclusion on the PDL.

LYLE LAIRD: A representative of Sunovia Pharmaceuticals discussed Latuda (Lorazadone Hydrochloride). Latuda is a newly approved atypical antipsychotic approved by the FDA on October 28 on first round approval. It is approved for the treatment of schizophrenia in adults. Schizophrenia is a chronic, progressive, neurodegenerative disorder that requires life-long treatment. Latuda offers a proven efficacy and safety profiles. Efficacy was established in four randomized double-blind placebo controlled, 6-week studies in adults with schizophrenia, which were reviewed. Latuda is available in 40- and 80-milligram tablets. It is dosed once daily. There is no dosage titration necessary. It is contraindicated in those who are hypersensitive to it. It is also contraindicated in those who are receiving CYP3A4 strong inducers or strong inhibitors. Latuda showed proven efficacy and safety in the clinical studies. The average weight gain in the short-term studies was just under a kilogram. In the uncontrolled longer studies, there was actually a mean weight decrease of almost a kilogram at week 52. It is associated with no clinically relevant mean changes in the metabolic parameters and serum glucose, total cholesterol and triglycerides in both the short-term studies and the long-term extensions. It is associated with no clinically relevant median changes in prolactin levels. It is a pregnancy category B. The most commonly observed adverse events, as well as the apparent dose-related events, were reviewed. Latuda carries a similar class warning and precaution as the other atypical antipsychotics, which were reviewed. There is no warning on QTC prolongation. Please consider including Latuda on the PDL.

In response to the committee's questions, Dr. Laid said Latuda would be available in the first quarter of 2011. It is not indicated in pediatrics, as the studies were in patients 18 years of age and older. Real world studies in cognition are an area of interest, but I do not know if there are studies planned.

DR. ESTHER ESTES: A representative of Merck discussed Saphris. Previously, Saphris was indicated for the treatment of schizophrenia in adults, as well as the treatment of manic episode associated with bipolar I disorder in adults. Since then, there have been two new studies resulting in an expanded indication. First was a maintenance trial in adult patients with schizophrenia, which was reviewed. The second study was an adjunctive trial in patients with manic or mixed episodes associated with bipolar I disorder in adults, which was reviewed. The updated label has Saphris

indicated for the treatment of schizophrenia, the acute treatment of manic or mixed episodes associated with bipolar I disorder, and as adjunctive therapy with either Lithium or Valproic acid for the treatment of manic or mixed episode associated with bipolar I disorder. In addition, there is now a new black cherry formulation. I would like to remind the committee that schizophrenia and bipolar I are a severe mental disorder and scientific understanding of these disorders is still in their infancy. Despite the treatment options, patients often relapse. The truth is we still do not know exactly how these treatments work. Health care providers should really have access to all treatment options available so they can manage this highly vulnerable population. I would ask the committee to maintain Saphris on the PDL.

DR. BARCEE (PH): A representative of AstraZeneca discussed Seroquel XR and Seroquel. Seroquel XR is FDA approved as adjunctive treatment in adults with major depressive disorder or MDD. Several trials and their outcomes were reviewed. Seroquel immediate release formulation is approved for the treatment of schizophrenia in adolescents 13 to 17 years old, and for the acute treatment of manic episodes associated with, bipolar I disorder in children and adolescents 10 to 17 years old. Seroquel should be administered to children and adolescents twice daily; however, it can be administered three times daily if needed. The recommended dosages were reviewed. Prescribing information for Seroquel XR and Seroquel contained the following boxed warnings. Elderly patients with dementia related psychosis treated with atypical antipsychotic drugs are at increased risk of death compared to placebo. Seroquel XR and Seroquel are not approved for the treatment of patients with dementia related psychosis. Antidepressants increase the risk of suicidal thinking and behavior in short-term studies in children, adolescents, and young adults with major depressive disorder and other psychiatric disorders. Seroquel is not approved for use in patients less than 10 years of age. Seroquel XR is not approved for use in patients less than 18 years of age. Prescribing information for Seroquel XR and Seroquel include warnings and precautions for neuroleptic malignant syndrome, hyperglycemia and diabetes, hyperlipidemia, (indiscernible) tardive dyskinesia, orthostatic hypotension, leukopenia, neutropenia, and agranulocytosis. Risk of cataracts, seizure, hypothyroidism, (indiscernible), potential for cognitive and motor impairment, body temperature dis-regulation, dysphasia, suicide, (indiscernible), and withdrawal. Prescribing information also includes a warning and precaution regarding increases in blood pressure in children and adolescents. Please refer to the full prescribing information for a list of adverse events.

DR. KIM LAUBMEIER: A representative of Bristol-Myers Squibb discussed Abilify (Aripiprazole). The safety and efficacy of Aripiprazole has been studied in multiple psychiatric diagnoses in adults and pediatric patients. The resulting 14 FDA approved indications are the treatment of schizophrenia in adults and adolescents age 13 to 17 years, acute and maintenance treatment of manic or mixed episodes associated with bipolar I disorder in adults and pediatric patients age 10 to 17 years, the use of adjunct therapy to antidepressants in adults with major depressive disorder who have had an inadequate response to prior antidepressant therapy, the treatment of irritability associated with autistic disorder in pediatric patients age 6 to 17 years, and finally the Aripiprazole IM formulation is indicated for the acute agitation associated with schizophrenia or bipolar I disorder in adults. According to surveillance data, approximately 75 percent of Aripiprazole prescriptions are for approved indications. The most recent efficacy data for Aripiprazole is in pediatric patients with autistic disorder and adult patients with major depressive disorder. Several trials and their outcomes were reviewed. The boxed warnings include increased mortality in elderly patients with dementia related psychosis and suicidality in antidepressant drugs. Please refer to the full package insert for Abilify, which is available online at abilify.com. Aripiprazole has a broad range of indications across adult and pediatric patients. As such, we respectfully request that Aripiprazole remain available on the PDL.

DR. FRED AMBERGER: A representative of Novartis discussed Fanapt. Fanapt tablets are indicated for the acute treatment of schizophrenia in adults. Approval of Fanapt was supported by two trials. Safety data was derived from more than 2,000 patients in short and long-term studies. Several trials and their outcomes were reviewed. Efficacy was demonstrated across doses of 12 to 24 milligrams per day, which is the recommended daily target dose range. Fanapt must be titrated slowly from a low stating dose to avoid orthostatic hypotension. Titration to the lowest effective dose of 12 milligrams per day can be achieved in four days with the use of an available titration pack. Fanapt should be given as a BID dose. The effectiveness of Fanapt for more than six weeks has not been systematically evaluated in clinical trials. Therefore, the physician who elects to use Fanapt for extended periods should periodically reevaluate the long-term usefulness of the drug for the individual patient. The most common adverse drug reactions were reviewed. In clinical trials, discontinuation rates due to side effects for patients on Fanapt and placebo were similar. A drug-drug interaction with CYP2D6 and 3A4 inhibitors requires the dose be reduced by about 50 percent. The incidents of feeling of inner restlessness often associated with other antipsychotics were also shown to be similar between placebo and Fanapt up to the maximum dose of 24 milligrams per day. Thirteen percent of patients taking Fanapt experienced a weight gain of 7 percent or more of body weight in clinical trials. Across all short and long-term studies, the overall mean weight gain from baseline to end of the trial was 2.1 kilograms. Patients did not experience medically important changes in triglyceride and total cholesterol measurements. Fanapt also demonstrated low incidents of extra pyramidal symptoms that were similar to placebo, which were reviewed. Consistent with class labeling for atypicals, Fanapt is not approved for the treatment of elderly patients, 65 and older, with psychosis related II dementia. Individuals with schizophrenia face enormous challenges. In addition, while there is no cure, it can be a manageable illness when a patient has the right medication. It is important to have a therapeutic option like Fanapt that can manage symptoms and enable functioning. For more information, please see the Fanapt package insert.

Dr. Pritchard read a letter from Dr. Curtiss, a former member of the committee, supporting all atypical antipsychotic medications on the PDL.

Dr. Brodsky suggested that those testifying could simply ask the committee to refer to the supplement and just list the black box warnings so more time could be available to review the drugs.

Dr. Pritchard gave the Magellen presentation on Atypical Antipsychotics. The atypical antipsychotic agents are serotonin and dopamine antagonists, although specific receptor binding and affinity varies widely between agents. There is less risk of EPS and improvement in both positive and negative symptoms of disease. The agents carry boxed warnings and new warnings have come out for most, which will be reviewed during the significant changes. In October, there were 4,531 claims: 23.42% for Seroquel, 22.16% for Abilify, 19.73% for Risperidone, 15.49% for Zyprexa, and all of the rest are under 10%. There were no prescriptions for Fanapt and for Saphris there were three prescriptions. At the last review, a motion for therapeutic alternatives with at least one entry from each class be included on the PDL passed with one opposed. The significant changes were reviewed. Fanapt was added to the market. Saphris and Fanapt have the QT prolongation. Saphris is not recommended for those with severe hepatic impairment. Patients taking Saphris should not eat or drink for 10 minutes following the dose. Fanapt dose should be reduced when in the presence of CYP2D6 or 3A4 inhibitors. Symbyax has warnings for serotonin syndrome, allergic reaction and rash, activation of mania and hypomania, and abnormal bleeding. Seroquel XR has withdrawal symptoms upon discontinuation, risk for cataracts,

hypothyroidism, and transaminase elevation. Latuda is due to come out on the market in February 2011. It is a second generation antipsychotic for use in adults with schizophrenia. It does carry the same boxed warnings as the others. Place in therapy is unknown at this time. There was no expert opinion on this class.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

15. Re-review of Progestins Used for Cachexia (Blue Category)

Dr. Pritchard gave the Magellen presentation on Progestins Used for Cachexia. There is one chemical entity and two products in this class. Both products are indicated for cachexia associated with AIDS. However, both are used to treat cachexia resulting from other conditions. In October, there were 2 claims for Megace ES. At the last review, a motion for class effect passed unanimously. The significant changes were reviewed. Chronic use of Megestrol is associated with new onset diabetes mellitus.

DR. PAPPENHEIM MOVED A CLASS EFFECT. SECONDED BY DR. CARLSON. THE MOTION PASSED UNANIMOUSLY.

16. Re-review of H2RAs (Blue Category)

Dr. Pritchard gave the Magellen presentation on H2RAs. All of the medications in this class have similar FDA indications and efficacy. The drug interaction profile of Cimetidine is concerning. In October, there were 892 claims: 70.18% for Ranitidine, 17.04% for Famotidine, and the rest were all less than 10%. At the last review, a motion for class effect to include at least one pediatric preparation passed with one opposed. The significant changes were reviewed. Impotence is reported with Famotidine, Ranitidine, and Nizatidine, but at similar frequency to placebo. There are rare cases of gynecomastia with these three drugs.

Dr. Liljegren said Cimetidine had been excluded from the PDL in the past and should remain excluded since it was an inferior drug due to side effects.

DR. DEMAIN MOVED A CLASS EFFECT, AND INCLUDE AT LEAST ONE PEDIATRIC PREPARATION AND TO EXCLUDE CIMETIDINE ON THE PDL. SECONDED BY DR. LILJEGREN. THE MOTION PASSED WITH ONE OPPOSED.

17. Re-review Urinary Tract Antispasmodics (Blue Category)

Dr. Pritchard gave the Magellen presentation on Urinary Tract Antispasmodics. There is one transdermal product and a topical gel. There is similar efficacy across class. The ADR profiles differ. There is better patient tolerability with the newer agents and dosage forms versus Oxybutynin. In October, there were 421 claims: 43.47% for Detrol LA, 14.01% for VESIcare, 11.64% for Enablex, and the rest were less than 10%. At the last review, a motion for class effect with one long-acting agent to be included passed unanimously. The significant changes were reviewed. Heat prostration due to decreased sweating may occur with anticholinergic drugs when in environments with excessive heat. The transfer of Oxybutynin can occur skin to skin with the transdermal form. Patients should wash

hands after application. Angioedema of face, lips, tongue and larynx can occur with first dose of VESIcare. There was a study comparing Toviaz to Detrol LA. Both are efficacious, but Toviaz has better response in urgency urinary incontinence.

DR. CARLSON MOVED A CLASS EFFECT WITH ONE LONG-ACTING AGENT TO BE INCLUDED ON THE PDL. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

18. Re-review of PPIs (Blue Category)

Dr. Pritchard gave the Magellen presentation on PPIs. FDA approved indications vary, but all drugs are used for all indications in clinical practice. ADR profiles and efficacy are similar across class. No studies reflect twice daily dosing works any better than once daily in patients who have an unsatisfactory response to once-daily dosing, but expert opinion does lean toward increasing to twice daily in these patients. If after twice daily dosing symptoms do not resolve then consider a treatment failure. In October, there were 2,088 claims: 37.74% for Nexium, 27.73% for Omeprazole Rx, 15.04% for Lansoprazole Rx, and the less were all less than 10%. At the last review, a motion for class effect with one pediatric appropriate agent to be included on the PDL passed unanimously. The significant changes were reviewed. Kapidex changed its name to Dexilant. Observational studies suggest that long-term, meaning longer than one year, high dose, meaning multiple daily doses, are associated with an increased risk of osteoporosis related fractures. There is a warning about using Omeprazole with Plavix. It is thought that this is related to CYP2C19 enzyme system. Nexium uses the same system. Although there are no warnings for Nexium and Plavix, this combination should not be used.

Dr. Demain discussed a New England Journal article that determined there was no increased risk with the PPIs in Plavix compared to clopidogrel. Dr. Pritchard said the FDA warning still stands.

In response to Dr. Michaud, Mr. Campana said the medically necessary clause could be used for pediatric formulations if a pediatric formulation was not preferred.

DR. LILJEGREN MOVED A CLASS EFFECT, AND ONE PEDIATRIC PREPARATION BE INCLUDED ON THE PDL. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.

In response to Dr. Brodsky, Mr. Campana said PPIs required prior authorizations, but they were considering implementing step edits. Omeprazole OTC is covered and does not require a prior authorization for the other PPIs.

19. Re-review of COX-2 Inhibitors (Green Category)

Dr. Pritchard gave the Magellen presentation on COX-2 Inhibitors. In October, there were 304 claims: 66.45% for Celebrex and 35.55% for Meloxicam tablets. At the last review, a motion for class effect passed unanimously.

DR. MICHAUD MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

20. Re-review of Skeletal Muscle Relaxants (Green Category)

Dr. Pritchard gave the Magellen presentation on Skeletal Muscle Relaxants. There are nine chemical entities in this class, many available branded and generic products. Three are available as combinations with aspirin. Cyclobenzaprine is available as an extended release product. Products in this class are either approved for adjunct treatment of acute painful muscular skeletal conditions or spasticity associated with motor neuron syndromes. In October, there were 1,187 claims: 59.31% for Cyclobenzaprine, 23.67% for Tizanidine, 21.15% for Baclofen, and the rest were all less than 10%. At the last review, a motion for class effect passed with three opposed. The significant changes were reviewed. Baclofen can be administered intrathecally, and Orphenadrine can be administered either intravenously or intramuscularly. The other agents are orally administered.

Dr. Liljegren did not feel the drugs were therapeutically equivalent, but were therapeutic alternatives. Baclofen has different indication than the other drugs.

DR. CARLSON MOVED A CLASS EFFECT. THERE WAS NO SECOND.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

21. Re-review Other Antidepressants (Green Category)

Dr. Pritchard gave the Magellen presentation on Other Antidepressants. In October, there were 1,653 claims: 45.67% for Trazodone, 11.62% for Mirtazapine, and all the rest were less than 10%. At the last review, a motion for therapeutic alternatives with no preference passed with three opposed. The significant changes were reviewed. Trazodone ER was added to the market as Oleptro. Trazodone and Bupropion are required by FDA to be dispensed with medication guide. Trazodone is associated with ejaculation disorders, erectile dysfunction, and decreased libido.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. MICHAUD. THE MOTION PASSED UNANIMOUSLY.

22. Re-review of SSRIs (Green Category)

Dr. Pritchard gave the Magellen presentation on SSRIs. There is similar efficacy between all of these agents. In October, there were 3,155 claims: 23.84% for Sertraline tablets, 23.2% for Fluoxetine capsules, 22.09% for Lexapro, 16.1% for Citalopram tablets, all the rest were less than 10%. At the last review, a motion for class effect to include at least one oral solution passed with one opposed.

DR. BRIGGS MOVED A CLASS EFFECT. SECONDED BY MR. GREEAR.

The committee discussed whether an approved drug would be provided in all forms. Mr. Campana said it depends on the exact bid from the manufacturer.

An unidentified female, a child psychiatrist, said she did not mind writing medically necessary on some preparations. However, she has a number of children on antidepressants that cannot take pills. Mr. Campana said generic Citalopram and Fluoxetine solutions were currently preferred and would probably remain on the PDL.

THE MOTION PASSED UNANIMOUSLY.

23. Re-review of Sedative Hypnotics (Green Category)

Dr. Pritchard gave the Magellen presentation on Sedative Hypnotics. There are two classifications, benzodiazepine or non-benzodiazepine. Rozerem has a unique mechanism in this class. In October, there were 1,184 claims: 45.27% for Zolpidem, 16.05% for Ambien, 15.37% for Temazepam, 11.74% for Lunesta, and all the rest were less than 10%. At the last review, a motion for therapeutic alternatives passed with one opposed.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. PAPPENHEIM.

Dr. Liljegren questioned if the committee wanted to include least one benzodiazepine and one non-benzodiazepine on the PDL. After reviewing the utilization list, Dr. Brodsky noted that more of the prescriptions were for non-benzodiazepines.

THE MOTION PASSED WITH ONE OPPOSED.

24. Re-review of ADD/ADHD (Green Category)

Dr. Pritchard gave the Magellen presentation on ADD/ADHD. Modafinil and Armodafinil do not have pediatric indications. The rest are used in both adults and children. There is similar efficacy between agents, but much variability in patient response. In October, there were 2,324 claims: 26.2% for Concerta, 12.56% for Dextro/Amphet capsule SR, 11.1% for Strattera, 10.03% for Focalin XR, the rest had less than 10%. At the last review, a motion for therapeutic alternatives with at least one extended release and one non-stimulant product passed. The significant changes were reviewed. Guanfacine ER (Intuniv) and Clonidine ER (Kapvay) are non-stimulant centrally acting alpha two adrenergic receptor agonists. These reduce sympathetic nerve impulses. It is not known how this mechanism works in ADHD, but the studies to date to show effectiveness. However, they are no more effective than other drugs used to treat this condition. Patients need to be tapered off these drugs. Provigil and Nuvigil can decrease the effectiveness of oral contraceptives so alternate methods of birth control need to be used while patients are on the drug and for one month after discontinuation.

DR. PHILLIPS MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES AND AT LEAST ONE EXTENDED RELEASE AND ONE NON-STIMULANT FORMULATION BE INCLUDED ON THE PDL. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

25. Re-review of Growth Hormones (Green Category)

Dr. Pritchard gave the Magellen presentation on Growth Hormones. All products are recombinant human growth hormone. Indications and delivery devices vary. In October, there were 18 claims: 50% for Nutropin AQ cartridge, 16.67% for Genotropin cartridge, 11.11% for Nutropin AQ vial, and the rest were less than 10%. At the last review, a motion for class effect passed unanimously. The significant changes were reviewed. There were no changes in the drug, just the delivery system. Nutropin AQ Newspin is available as a pre-filled cartridge with a reusable multi-dose injection device. Tev-Tropin T-Jet is available as a needle-free alternative. It works as via rapid pulse fluid stream, but you still have to draw the dose from the vial.

DR. PHILLIPS MOVED A CLASS EFFECT. SECONDED BY DR. MICHAUD. THE MOTION PASSED WITH ONE ABSTENTION.

26. Review Minutes from September 2010 Meeting

Mr. Campana reviewed the corrections to September 2010 meeting minutes.

DR. PAPPENHEIM MOVED TO APPROVE THE SEPTEMBER 2010 MEETING MINUTES AS CORRECTED. SECONDED BY DR. MICHAUD. THE MOTION PASSED UNANIMOUSLY.

27. Comments from Committee Members or Chair

The next meeting is scheduled for January 21, 2011.

28. Adjourn

The meeting adjourned at 11: 13 a.m.